

Hepatitis A Virus in Transplants

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Today I'm talking with Dr. Monique Foster, a CDC scientist, about her article on hepatitis A and transplants. We're glad to have you here with us today Dr. Foster.

[Monique Foster] Hi Sarah, thanks so much for having me.

[Sarah Gregory] There are so many variants of hepatitis now. What is hepatitis A?

[Monique Foster] Yeah sure, so hepatitis A is a small, RNA virus that causes inflammation of the liver. It clinically causes symptoms similar to the other viral hepatitis viruses, most notably hepatitis B, C, and hepatitis E. What makes hepatitis A virus unique compared to the hepatitis B and C viruses, is that it typically causes an acute, or short term, illness. There's typically no chronic, or on-going form of this disease.

[Sarah Gregory] Does it impact many people globally?

[Monique Foster] Hepatitis A virus is the most common form of acute viral hepatitis worldwide. It is estimated that 1.5 million cases of hepatitis A virus infection occur globally each year, but due to underreporting and asymptomatic infections in children, the true number of infections may actually be up to ten-times that number.

[Sarah Gregory] How do people usually get it?

[Monique Foster] So, the virus is spread fecal-orally, when humans consume, usually microscopic amounts, of human feces. Typically the virus spreads from person-to-person, but can also cause foodborne and/or waterborne outbreaks when that fecal matter contaminates food or water sources. It is uncommon to see outbreaks of hepatitis A virus due to contaminated water here in the United States because adequate chlorination kills the virus. Foodborne outbreaks still occur occasionally and the last three large foodborne outbreaks that have occurred over the last five years have been linked to foods imported from countries where hepatitis A virus is endemic.

[Sarah Gregory] Tell us about your study?

[Monique Foster] Our study was an investigation into how two home health nurses became infected with hepatitis A virus. Infection with hepatitis A is a reportable disease in all states, so local and state health departments will typically interview cases when they receive a notification of a positive hepatitis A test. It was noted that these two nurses did not have common risk factors associated with hepatitis A infection, such as international travel, but did work for the same home health company and had taken care of the same patient. That patient had undergone liver, pancreas, and small bowel transplantation the year prior. Due to the long shifts in the household which included using shared restrooms and eating areas, the nurses were not just considered health care workers, but household contacts of this shared patient, so it was hypothesized that they were infected by someone within the household. Previous studies have shown that length of contact with an infected patient increases the likelihood of health care workers becoming infected, and post-exposure prophylaxis is recommended for household contacts of any infected patient. Later, a nurse who took care of the patient in the hospital, was also discovered to be

infected with hepatitis A. Initially the transplant recipient, who was the shared patient, was ruled out because of history of adequate vaccination with the hepatitis A vaccine as part of childhood vaccination, many years before the transplantation took place. The study describes the investigation and our findings.

[Sarah Gregory] It seems this study revealed some pretty interesting findings. What did you discover?

[Monique Foster] There were multiple surprising findings during this investigation. After ruling out both the patient's parents as the possible source of the hepatitis A virus infections, the transplant recipient was tested and found to be infected, despite having been vaccinated previously and having no risk factors for infection. At this point, the next step in the investigation was to determine exactly when she became infected and then determine exposures during her incubation period. One of the organs that the transplant recipient received was a liver, which is the organ in the body where the virus replicates, so determining when the patient became infected was complicated by the clinical similarities of hepatitis A virus infection to acute liver rejection.

[Sarah Gregory] Wasn't there something unusual about the incubation period of the virus in the recipient?

[Monique Foster] The incubation period for hepatitis A virus is relatively long—it's 15 to 50 days—but the time period during which someone experiences symptoms and has virus present in his or her blood and stool, and is therefore contagious, is relatively short—two to four weeks. Because of the difficulty in determining acute hepatitis A virus infection versus acute liver rejection, we had to rely on laboratory testing of tissue, blood, and stool to further narrow the date when the patient was infected and then we would be able to examine exposures during the incubation period, which again was 15 to 50 days before that date, to determine the source of the infection. We obtained specimens of her original liver, transplanted liver, and transplanted small bowel, from the time during her transplantation and were surprised to discover that her native liver was not infected with the virus, but her transplanted liver showed detectable virus just 5 days after transplantation. Since there was a possibility that the source of the infection was the organ transplantation, we tested serum from the organ donor and were surprised to find the presence of hepatitis A virus. Genetic testing of the virus recovered from the transplant donor, recipient, and health care workers who took care of the organ recipient in her home and in the hospital, revealed that all were infected with genetically identical virus which confirmed transmission from the donor to the recipients and then on to the nurses. While hepatitis A virus infection after blood transfusion has been described previously, there was nothing in the medical literature that reported hepatitis A virus transmission by solid organ transplantation.

The incubation period for the transplant recipient was likely the same as for anyone, but laboratory testing has shown that the transplant recipient had virus present in her blood for almost a year, and in her stool for 15 months, making her infectious for as long as the virus was present. Those are very long times to be infectious when a typical person infected with hepatitis A virus is infectious for two to four weeks.

[Sarah Gregory] I understand the health care workers also got it. How did this happen?

[Monique Foster] Since the primary transmission of hepatitis A virus is fecal–oral, it is not surprising that diarrhea or fecal incontinence leads to the spread of infection. In this case, the organ recipient had an ileostomy and colostomy, which are surgical openings which bring the small intestine and colon onto the surface of the skin where a bag collects intestinal waste. Output of waste had increased from these openings as you would see in what we would define as “diarrhea,” but it was difficult to determine whether these increases represented symptoms from hepatitis A virus infection because her output was always described as continuously liquid, even before her hepatitis developed. Outbreaks in hospitalized settings are uncommon because hygienic practices are generally adhered to more consistently when the patient is symptomatic enough to be hospitalized. The use of contact precautions is recommended for health care workers caring for patients with hepatitis A virus who are diapered or incontinent, but during the many times the patient was hospitalized after the transplantation, her hepatitis A virus infection was unknown. Because health care workers do not have increased prevalence of hepatitis A virus infection and because nosocomial outbreaks of hepatitis A virus are rare, hepatitis A vaccination is not mandatory for health care workers in the United States. Once the infection was detected, contact precautions were instituted during subsequent hospitalizations, and the local health department recommended the patient’s home health nurses be fully vaccinated against the virus, and no further transmissions to health care workers were detected during the subsequent eight months of continued viral shedding in the patient’s feces.

[Sarah Gregory] Why was the diagnosis of hepatitis A in the patient delayed?

[Monique Foster] While elevated liver enzymes, increased bilirubin, jaundice, and diarrhea are seen with both hepatitis A virus infection and acute liver rejection, and with the patient’s history of hepatitis A vaccination, her symptoms were attributed to possible liver rejection at that time. Symptomatic persons typically show elevated liver enzyme levels that coincides with their onset of clinical illness. The infected organ recipient had elevated liver enzymes shortly after her liver transplantation, but this coincided with other viral infections and was later assumed to be related to her possible organ rejection.

[Sarah Gregory] Was there a way this transmission could have been prevented?

[Monique Foster] The most effective way to prevent this unlikely chain of events would have been for the organ donor to have been vaccinated against hepatitis A virus infection as a part of his routine childhood immunizations. In 2006, the Advisory Committee on Immunization Practices recommended routine hepatitis A vaccination for all children beginning at between 12 and 23 months of age. Both inactivated whole-virus vaccines available in the United States are well tolerated and effective, showing levels of protection for at least 17 years. In 2014, two-dose vaccination coverage among children aged 19 to 35 months in the United States was only around 58 percent, and that’s the lowest vaccine coverage for a complete vaccine series among all the routine childhood vaccines.

[Sarah Gregory] Care to tell me about your job and why you were interested in doing this study?

[Monique Foster] Sure. Currently I am one of the hepatitis A virus subject matter experts in the Division of Viral Hepatitis. I started out at CDC as an Epidemic Intelligence Service Officer, also in the Division of Viral Hepatitis. I thought my experience as an EIS officer within this division gave me a pretty well-rounded experience of applied epidemiology. I investigated

multiple outbreaks, including this one, analyzed data, and evaluated public health programs. Investigating hepatitis A virus outbreaks are always a challenge due to the long incubation period and the virus being able to survive different environmental conditions, such as freezing, drying on surfaces, and acidic environments. Doing this study, we discovered that it is possible for hepatitis A virus to be transmitted via solid organ transplantation and we reiterate the importance of childhood hepatitis A vaccination.

[Sarah Gregory] Thank you so much for taking the time to talk with me today, Dr. Foster. Listeners can read the entire April 2017 article, Transmission of Hepatitis A Virus through Combined Liver-Small Intestine-Pancreas Transplantation, at CDC.gov/EID.

I'm Sarah Gregory for *Emerging Infectious Diseases*.

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.